

RESPONSE TO RESTRICTION AND ELECTION OF SPECIES REQUIREMENTS AND
SECOND PRELIMINARY AMENDMENT

Attorney Docket No.: Q92245

U.S. Application No.: 10/561,973

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application:

LISTING OF CLAIMS:

1. **(withdrawn)** A compound represented by formula (I)



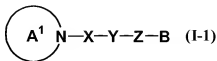
wherein A is a cyclic group which may have a substituent(s);

X, Y and Z are each independently a single bond or a spacer of which main chain has an atom number of 1-3; and

B is a hydrocarbon group which may have a substituent(s) or a cyclic group which may have a substituent(s),

a salt thereof, an N-oxide thereof, a solvate thereof or a prodrug thereof.

2. **(withdrawn)** The compound according to claim 1, which is represented by formula (I-1)



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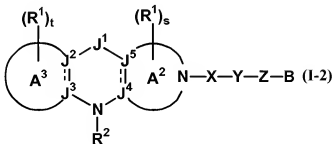
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wherein ringA¹ is a di-, tri-, or tetra-nitrogen-containing heterocyclic ring, the other symbols have the same meanings as those defined in claim 1, and wherein ringA¹ is not 2,3,4,5-tetrahydro-1H-1-benzazepine, 1,2,3,4,5,6-hexahydro-1-benzazepine, 2,3,4,5-tetrahydro-1,5-benzoxazepine, 6,7,8,9-tetrahydro-5H-pyrid[2,3-d]azepine or 5,6,7,8-tetrahydro-4H-thieno[3,2-d]azepine.

3. **(withdrawn - Currently Amended)** The compound according to claim 2, wherein ringA¹ is a tri-, or tetra-nitrogen-containing heterocyclic ring.

4. **(withdrawn)** The compound according to claim 3, which is represented by formula (I-2)



wherein ringA² is a mono-nitrogen-containing heterocyclic ring;

ringA³ is a mono-carbocyclic ring or mono-heterocyclic ring;

plural R¹'s are each independently a substituent, and when R¹'s are plural, two R¹'s may be together to form cyclic group which may have a substituent(s);

R² is a hydrogen atom or a substituent;

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t and s are each independently 0 or an integer of 1-5, and the sum of t and s is 5 or less;

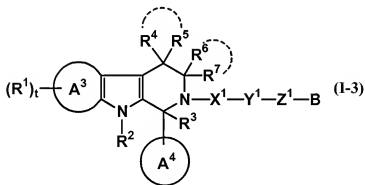
J¹ is a single bond, a carbon atom which may have a substituent(s), a nitrogen atom which may have a substituent(s), an oxygen atom or a sulfur atom which may be oxidized;

J², J³, J⁴ and J⁵ are each independently a carbon atom or a nitrogen atom,

----- is a single bond or a double bond, and

the other symbols have the same meanings as those defined in claim 1.

5. **(withdrawn)** The compound according to claim 4, which is represented by formula
(I-3)



wherein R³, R⁴, R⁵, R⁶ and R⁷ are each independently a hydrogen atom or a substituent, and R⁴ and R⁵, and/or R⁶ and R⁷ may be together with their binding carbon atom to form a cyclic group which may have a substituent(s);

ring A⁴ is a cyclic group which may have a substituent(s);

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X^1 and Z^1 are each independently a single bond, C1-3 alkylene which may have a substituent(s), C2-3 alkenylene which may have a substituent(s) or C2-3 alkynylene which may have a substituent(s);

Y^1 is $-C(=O)-$, $-C(=S)-$, $-C(=O)NR^{103}-$, $-SO_2-$, $-C(=O)O-$ or $SO_2NR^{103}-$, in which R^{103} is a hydrogen atom or a substituent,

the sum of the number of substituents represented by R^1 , R^3 , R^4 , R^5 , R^6 and R^7 is 4 or less, and

the other symbols have the same meanings as those defined in claim 1.

6. **(withdrawn)** The compound according to claim 5, wherein R^4 and R^5 are simultaneously substituents, or R^4 and R^5 are together with their binding carbon atom to form a cyclic group which may have a substituent(s).

7. **(withdrawn)** The compound according to claim 5, wherein R^3 is a substituent.

8. **(withdrawn)** The compound according to claim 5, wherein R^6 and R^7 are simultaneously substituents, or R^6 and R^7 are together with their binding carbon atom to form a cyclic group which may have a substituent(s).

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9. **(withdrawn)** The compound according to claim 5, wherein R³ is a mono-heterocyclic ring.

10. **(withdrawn)** The compound according to claim 5, wherein B is a C3-10 mono-, or di-carbocyclic ring which may have a substituent(s) or a 3-10 membered mono-, or di-heterocyclic ring which may have a substituent(s).

11. **(withdrawn)** The compound according to claim 5, wherein ringA⁴ is a C3-10 mono-, or di-carbocyclic ring which may have a substituent(s) or a 3-10 membered mono-, or di-heterocyclic ring which may have a substituent(s).

12. **(withdrawn)** The compound according to claim 5, wherein Y¹ is -C(=O)- or -C(=O)NR¹⁰³-.

13. **(withdrawn)** The compound according to claim 4, which is selected from

- (1) N-(3,5-dimethylphenyl)-1,3,4,9-tetrahydro-2H- β -carboline-2-carboxamide,
- (2) N-(3-methylphenyl)-1,3,4,9-tetrahydro-2H- β -carboline-2-carboxamide,
- (3) N-(3,5-dimethylphenyl)-6-methoxy-1,3,4,9-tetrahydro-2H- β -carboline-2-carboxamide,

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- (4) 6-methoxy-N-(3-methylphenyl)-1,3,4,9-tetrahydro-2H- β -carboline-2-carboxamide,
- (5) 6-methoxy-N-[2-(trifluoromethyl)phenyl]-1,3,4,9-tetrahydro-2H- β -carboline-2-carboxamide,
- (6) N-(3,5-dichlorophenyl)-6-methoxy-1,3,4,9-tetrahydro-2H- β -carboline-2-carboxamide,
- (7) 1-(3-fluorophenyl)-N-phenyl-1,3,4,9-tetrahydro-2H- β -carboline-2-carboxamide,
- (8) 1-(3-fluorophenyl)-N-(3-methylphenyl)-1,3,4,9-tetrahydro-2H- β -carboline-2-carboxamide,
- (9) N-(3,5-dimethylphenyl)-1-(3-fluorophenyl)-1,3,4,9-tetrahydro-2H- β -carboline-2-carboxamide,
- (10) 2-acetyl-1-(3-fluorophenyl)-2,3,4,9-tetrahydro-1H- β -carboline,
- (11) 2-({[5-(trifluoromethyl)pyridin-2-yl]thio}acetyl)-2,3,4,9-tetrahydro-1H- β -carboline,
- (12) 2-({[2,5-dimethoxyphenyl]thio}acetyl)-2,3,4,9-tetrahydro-1H- β -carboline,
- (13) 6-methoxy-1-(trifluoromethyl)-2-({[5-(trifluoromethyl)pyridin-2-yl]thio}acetyl)-2,3,4,9-tetrahydro-1H- β -carboline,
- (14) 2-({[2,5-dimethoxyphenyl]thio}acetyl)-6-methoxy-1-(trifluoromethyl)-2,3,4,9-tetrahydro-1H- β -carboline,

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(15) 6-methoxy-N-(3-methylphenyl)-1-(trifluoromethyl)-1,3,4,9-tetrahydro-2H- β -carboline-2-carboxamide,

(16) N-(3,5-dimethylphenyl)-1-(3-fluorophenyl)-1,9-dihydrospiro[β -carboline-4,1'-cyclopropane]-2(3H)-carboxamide,

(17) rac-(1R,3S)-N-(3,5-dimethylphenyl)-1-(3-fluorophenyl)-3-methyl-1,3,4,9-tetrahydro-2H- β -carboline-2-carboxamide,

(18) rac-(1R,3R)-N-(3,5-dimethylphenyl)-1-(3-fluorophenyl)-3-methyl-1,3,4,9-tetrahydro-2H- β -carboline-2-carboxamide,

(19) N-(3,5-dimethylphenyl)-1-(3-fluorophenyl)-6-(trimethylsilyl)-1,3,4,9-tetrahydro-2H- β -carboline-2-carboxamide,

(20) N-(3,5-dimethylphenyl)-1-(3-fluorophenyl)-4,4-dimethyl-1,3,4,9-tetrahydro-2H- β -carboline-2-carboxamide,

(21) 2-acetyl-1-(3-fluorophenyl)-1,2,3,9-tetrahydrospiro[β -carboline-4,1'-cyclopropane],

(22) 2-(benzylsulfonyl)-1-(3-fluorophenyl)-2,3,4,9-tetrahydro-1H- β -carboline,

(23) rac-(1R,3R)-2-acetyl-1-(3-fluorophenyl)-3-methyl-2,3,4,9-tetrahydro-1H- β -carboline,

(24) methyl 1-(3-fluorophenyl)-3,3-dimethyl-1,3,4,9-tetrahydro-2H- β -carboline-2-carboxylate, and

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(25) N-(3,5-dimethylphenyl)-8-(3-fluorophenyl)-5,6,8,9-tetrahydro-7H-pyrido[4',3':4,5]pyrrolo[2,3-b]pyridine-7-carboxamide.

14. **(currently amended)** A pharmaceutical composition comprising the compound represented by formula (I) according to claim 4-23, a salt thereof, an N-oxide thereof, a solvate thereof or a prodrug thereof.

15. **(original)** The pharmaceutical composition according to claim 14, which is a preventive and/or therapeutic agent for a mitochondrial benzodiazepine receptor mediated disease.

16. **(original)** The pharmaceutical composition according to claim 15, wherein the mitochondrial benzodiazepine receptor mediated disease is a disease caused by stress.

17. **(original)** The pharmaceutical composition according to claim 16, wherein the disease caused by stress is a central nervous system disease caused by stress, a respiratory system disease caused by stress and/or a digestive system disease caused by stress.

18. **(original)** The pharmaceutical composition according to claim 17, wherein the central nervous system disease caused by stress is anxiety-related disease, sleep disorder,

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depression and/or epilepsy; a respiratory system disease caused by stress is asthma; or the digestive system disease caused by stress is irritable bowel syndrome.

19. **(Withdrawn)** A method for prevention and/or treatment for a central nervous system, a respiratory system disease and/or a digestive disease in mammals, comprising administering to a mammal an effective amount of the compound represented by formula (I) according to claim 1, a salt thereof, an N-oxide thereof, a solvate thereof or a prodrug thereof.

20. **(Withdrawn)** A pharmaceutical composition combining the compound represented by formula (I) according to claim 1, a salt thereof, an N-oxide thereof, a solvate thereof or a prodrug thereof, and one kind or more kind selected from antianxiety drugs, antidepressant drugs, antiparkinson drugs, therapeutic drugs for schizophrenia, antiepileptic drugs, therapeutic drugs for asthma, therapeutic drugs for peptic ulcer, adjustive drugs for gastrointestinal function, antidiarrheals, evacuants, antihypertensive drugs, antiarrhythmic drugs, inotropic drugs and therapeutic drugs for urination disorder.

21. **(Withdrawn-currently amended)** A method for prevention and/or treatment for a mitochondrial benzodiazepine receptor mediated disease in mammals, which comprises administering to a mammal an effective amount of the compound represented by formula (I) according to claim 423, a salt thereof, an N-oxide, a solvate or a prodrug thereof.

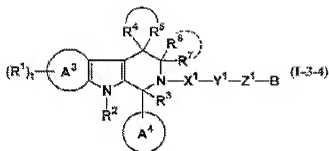
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22. (canceled)

23. (new): A compound represented by formula (I-3-4):



wherein,

ring A³ is benzene, pyridine, pyrimidine or pyrazine;

ring A⁴ is benzene which may be substituted with 1 to 4 substituent(s) optionally selected from C1-8 alkyl, C2-8 alkenyl, C2-8 alkynyl, a carbocyclic ring, a heterocyclic ring, hydroxyl, C1-8 alkoxy, amino, NR¹⁰⁴R¹⁰⁵, carboxyl, C1-6 alkoxy-carbonyl, nitro, cyano, a halogen atom, oxo, acyl, formyl and tri(C1-6 alkyl)silyl;

R¹⁰⁴ and R¹⁰⁵ are each independently a hydrogen atom or C1-8 alkyl;

R¹ is C1-8 alkyl, C2-8 alkenyl, C2-8 alkynyl, a carbocyclic ring which may have a substituent(s), a heterocyclic ring which may have a substituent(s), hydroxyl, C1-8 alkoxy, mercapto, C1-8 alkylthio, amino, NR¹⁰⁴R¹⁰⁵, carboxyl, C1-6 alkoxy-carbonyl, nitro, cyano, a halogen atom, oxo, acyl, formyl or tri(C1-6 alkyl)silyl;

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R^2 , R^3 , R^6 and R^7 are each independently C1-8 alkyl, C2-8 alkenyl, C2-8 alkynyl, a carbocyclic ring, a heterocyclic ring, hydroxyl, C1-8 alkoxy, mercapto, C1-8 alkylthio, amino, $NR^{104}R^{105}$, carboxyl, C1-6 alkoxy carbonyl, nitro, cyano, a halogen atom, oxo, acyl, formyl or tri(C1-6alkyl)silyl;

R^4 and R^5 are together with their binding carbon atom to form C3-8 cycloalkyl which may be substituted with 1 to 4 substituent(s) optionally selected from C1-8 alkyl, C2-8 alkenyl, C2-8 alkynyl, a carbocyclic ring, a heterocyclic ring, hydroxyl, C1-8 alkoxy, amino, $NR^{104}R^{105}$, carboxyl, C1-6 alkoxy carbonyl, nitro, cyano, a halogen atom, oxo, acyl, formyl and tri(C1-6 alkyl)silyl;

X^1 and Z^1 are each independently a single bond or C1-3 alkylene which may have a substituent(s);

Y^1 is $-C(=O)-$, $-C(=S)-$, $-C(=O)NR^{103}-$, $-C(=S)NR^{103}-$, $-SO_2-$, $-C(=O)O-$ or SO_2NR^{103} ;

R^{103} is a hydrogen atom or a substituent;

B is C1-8 alkyl, C2-8 alkenyl or C2-8 alkynyl which may be substituted with 1 to 4 substituent(s) optionally selected from hydroxyl, mercapto, amino, carboxyl, nitro, cyano, mono- or di-C1-6 alkylamino, C1-6 alkoxy, C1-6 alkylcarbonyloxy, C1-6 alkylthio, a halogen atom, acyl, a carbocyclic ring which may have a substituent(s), a heterocyclic ring which may have a substituent(s), or benzene which may be substituted with 1 to 4 substituent(s) optionally selected from C1-8 alkyl, C2-8 alkenyl, C2-8 alkynyl, a carbocyclic ring, a heterocyclic ring, hydroxyl,

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C1-8 alkoxy, amino, $\text{NR}^{104}\text{R}^{105}$, carboxyl, C1-6 alkoxy carbonyl, nitro, cyano, a halogen atom, oxo, acyl, formyl and tri(C1-6 alkyl)silyl; and

t is 0 or an integer 1 to 5, a salt thereof, an N-oxide thereof, a solvate thereof, or a prodrug thereof.

24. **(new)** The compound according to claim 23, wherein ring A³ is a benzene; Y¹ is -C(=O)- or -C(=O)NR¹⁰³-.

25. **(new)** The compound according to claim 23, which is selected from
(1) N-(3,5-dimethylphenyl)-1-(3-fluorophenyl)-1,9-dihydrospiro[β -carboline-4,1'-cyclopropane]-2(3H)-carboxamide, and

(2) 2-acetyl-1-(3-fluorophenyl)-1,2,3,9-tetrahydrospiro[β -carboline-4,1'-cyclopropane].